REMARKS

Applicants thank the Examiner for the courteous and helpful discussions held on April 29 and April 30, 2009. During those discussions, the Examiner and Applicants' representative discussed the claim amendments presented herein as well as the cited references of record.

In the Claims:

Claims 3 and 24 are amended herein. No new matter is added by this amendment and support for the amendment may be found throughout the specification, including at paragraphs 0002, 0005, 0017, 0024, 0025, 0032, 0033, Table 1 on page 6 and original claims 10, 12, 15, 18, and 21.

Claim 26 is newly added herein. No new matter is added by new claim 26 and support for claim 26 may be found throughout the specification, including at paragraphs 0002, 0005, 0017, 0024, 0025, 0032, 0033, and at Table 1 on page 6.

Claims 3, 6, 7, and 23-26 are currently pending.

Claim Rejections:

35 U.S.C. § 112, ¶ 1:

Claims 3, 6, 7, and 23-25 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office action alleges that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors were in possession of the claimed invention, because the phrase "a standardized concentration of the marker compound that is used to prepare an extract . . ." as present in claims 3 and 24 is alleged to be new matter. Specifically, the Office action alleges that the phrase is considered

new matter because "there is nowhere in the specification which teaches that the maturation stage *is selected* with a standardized concentration of the marker compound." (Office action dated February 2, 2009, p. 2). According to the Office action, "[t]he natural content of the chicoric acid is not considered 'standardization'; rather standardization is what occurs after the extract is collected; it is a means for manipulating the extract to contain certain levels of a compound." (Office action dated February 2, 2009, p. 3).

Applicants respectfully disagree with this ground of rejection. To expedite prosecution, Applicants have herein clarified the claims without disclaimer or prejudice. Specifically, Applicants have clarified that the phrase "a standardized concentration of the marker compound that is used to prepare an extract of the *Echinacea* plant" refers to "a standardized concentration of at least about 3.16% of either chlorogenic acid or chicoric acid as measured by high performance liquid chromatography analysis." No new matter is encompassed by this phrase.

Specifically, at paragraph [0002], the specification reports "Typically *Echinacea* extracts are standardized to contain a known concentration of one or more of chicoric acid, polysaccharides, or alkylamides." At the time of filing, one of ordinary skill in the art would recognize chlorogenic acid as a common marker compound of *Echinacea* plants. *E.g.* Rininger *et al.,* "Immunopharmacological activity of *Echinacea* preparations following simulated digestion on murine macrophages and human peripheral blood mononuclear cells." 2000. *J. Leukocyte Biol.,* Vol. 68, pp. 503-510, at pp. 507, 509.

At paragraph [0005], the specification states "Still another embodiment of the invention described herein is an *Echinacea* preparation that has a standardized concentration of chicoric acid." The specification similarly teaches "Chicoric acid is a preferred marker compound for *Echinacea purpurea* preparations" at paragraph [0017]. Indeed, original claims 10, 12, 15, 18, and 21 all contain the phrase "a standardized concentration of chicoric acid." In fact, original claim 21

requires "a standardized level of chicoric acid of at least about 3.49 percent as measured by HPLC analysis."

Paragraph [0025] explains that "standardization to a marker such as chicoric acid is important to meet market or regulatory expectations." Importantly, contrary to the argument at page 5 of the Office action mailed 2/2/09, paragraph [0024] teaches that *Echinacea* plants used in the claimed methods are chosen based on the amount of chicoric acid by contrasting the levels of chicoric acid measured during maturation stages 1-6 for *Echinacea purpurea* with those at maturation stage 7. For example, paragraph [0024] reports that "*Echinacea* plants harvested during maturation stage 7 are less commercially desirable due to the drop in the levels of chicoric acid observed at this stage." Paragraph [0004] reports that "[p]referably the *Echinacea* plant is harvested during or prior to stage 6 maturation. Stage 6 is characterized by erect ligular flowers that may be green or white in color. More preferably, the *Echinacea* plant is harvested during or prior to stage 3 maturation as characterized by the plant having a diminutive bud size of about 18 mm. Most preferably, the plant is harvested during the vegetative stage (maturation stage 1). The chicoric acid levels at maturation stages 1-7 are reported at Table 1.

Paragraph [0032] teaches that the levels of chicoric acid must be considered in connection with immune-stimulatory ability of extracts:

> The chicoric acid levels of stages 1, 3, and 6 do not vary considerably, see Table 1. The results depicted in Figure 1 indicate that while the levels of a standardization marker do not varying (*sic*) remarkably between maturation stages, immune-stimulatory induction vary a great deal based on the maturation stage during which the plant was harvested. Harvesting *Echinacea* plants prior to full bloom for use in products intended to stimulate the immune system does not interfere with currently practiced standardization procedures, but may provide for a greater immune-stimulatory effect."

Thus, Applicants respectfully submit that the phrase "a standardized concentration of the marker compound, wherein the marker compound is either chlorogenic acid or chicoric acid" presents no new matter and this ground of rejection is overcome. Applicants respectfully request it be withdrawn.

35 U.S.C. § 103(a)

Claims 3, 6, 7, 23 and 24 remain rejected under 35 U.S.C. 103(a) as being unpatentable over A in view of C in view of D in view of E or B in view of C in view of D in view of E, wherein A = Seidler-Lozykowska et al. (2003), B = Dou et al. (2001 – Abstract), C = Rininger et al. (2000), D = Wyllie et al (US 2003/0235890) and E = Gahler et al. (US 6,511,683).

Applicants respectfully disagree. According to Section 2141 of the MPEP, which is consistent with the Supreme Court's decisions in *Graham v. John Deere Co.,* 148 USPQ 459 (U.S. 1966) and *KSR Int'l Co. v. Teleflex Inc.*, 82 USPQ 2d 1385 (U.S. 2007), when determining whether a claimed invention is obvious under 35 U.S.C. § 103, the following tenets of patent law must be adhered to:

> (A) The claimed invention must be considered as a whole;
>
> (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
>
> (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
>
> (D) Reasonable expectation of success is the standard with which obviousness is determined.

Hodosh v. Block Drug Co., 786 F.2d 1136, 1143 n.5, 229 USPQ 182, 187 n.5 (Fed. Cir. 1986). These tenets of patent law are consistent with the *Graham* factors considered by the Office as indicated at page 9 of the Office action mailed 2/2/09.

When these tenets of patent law are properly applied, and the *Graham* inquiries are considered, it is clear that the claimed invention is not obvious in view of the cited references.

The Claimed Invention

In line with the first tenant of patent law, the claimed invention as a whole is a method for determining optimal harvest window of *Echinacea* based on selecting a plant maturation stage that has both a standardized concentration of either chicoric acid or chlorogenic acid and immunostimulatory activity. The claimed method also includes a step of preparing a standardized extract at that selected maturation stage.

According to the Office action, "there is no novel step or idea in the method claims which makes it unobvious over the prior art references." Office action mailed 2/2/09 at page 10. The Office action acknowledges that "no one, individual reference taught all of [the claimed] claimed steps together" but further argues that "the ordinary artisan would have been motivated to perform the claimed method in order to optimize the medicinal efficacy of an *Echinacea* extract and standardization would have been routine." *Id.* As explained below, Applicants respectfully disagree that the cited references demonstrate one of ordinary skill in the art would have been motivated to perform the claimed method because the cited references teach that when *Echinacea* extracts are standardized using chicoric acid or chlorogenic acid as marker compounds, the *Echinacea* extracts do not exhibit immunostimulatory activity.

The Cited References

The scope and content of the prior art, which includes the cited references, does not teach the claimed method. Instead, as previously argued (*see e.g.* Amendment and Response filed 10/9/08 at pages 9-11), the cited references teach away from the claimed method because as a whole, the cited references teach that when *Echinacea* extracts are standardized using chicoric acid or

chlorogenic acid as marker compounds, the *Echinacea* extracts do not exhibit immunostimulatory activity.

The Office action however, alleges "Applicants have not provided substantiating evidence to verify that the prior art in fact 'teaches away' from the claimed invention." Page 11 of the Office action mailed 2/2/09. According to the Office action, Gahler teaches that "[m]aturation stages of *Echinacea* were clearly recognized to produce varying levels of immunopotentiating activity." Page 12 of the Office action mailed 2/2/09. However, the portion of Gahler cited by the Office action does not teach how to select a maturation stage that comprises immune-stimulatory activity and a standardized concentration of a marker compound.

Indeed, although Gahler recognizes the need and advantage of standardizing *Echinacea* extracts to obtain optimized medicinal potential, Gahler, also teaches that using any marker compound alone, and specifically chicoric acid alone, will not result in any significant immunostimulatory activity. Specifically, Gahler teaches that immune enhancing activity is only observed when a number of marker compounds are used in combination with each other. For example, Gahler teaches that using chicoric acid, alkylamides and polysaccharides together as marker compounds enhances macrophage phagocytic activity and TNF-α production. (Col. 16, ll. 37-61). But, Gahler goes on to teach that an *Echinacea* extract standardized with primarily chicoric acid as the marker compound or polysaccharides as the marker compound do not display significant immunostimulatory activity. (Col. 24, ll. 29-38). Specifically, Gahler states, "Echinacea chicoric acid extract of the invention . . . had no significant effect on the phagocytic activity or the phagocytic index of rat alveolar macrophages. . . . Similarly . . . an *Echinacea* polysaccharide extract of the invention . . . had no significant effect on the phagocytic activity or the phagocytic index of rat alveolar macrophages." *Id.* Gahler further teaches that "Echinacea chicoric acid and polysaccharide extracts . . . did not significantly increase the level of nitric oxide production by alveolar macrophages." (Col. 24, ll. 64-67). Furthermore, Gahler

explains, "Echinacea chicoric acid extract . . . did not significantly increase the level of TNF-α production by alveolar macrophages." (Col. 25, ll. 15-18). Neither did *Echinacea* chicoric acid extracts or polysaccharide extracts "cause a significant increase in IFN-γ production by the splenocytes" (Col. 25, ll. 35-37), nor did they "affect the production of IL-2 in splenocytes." (Col. 26, ll. 4-7). Thus, one of ordinary skill in the art would understand from Gahler that some *Echinacea* extracts standardized by multiple marker compounds can be harvested at certain maturation stages to optimize immunostimulatory activity, but that *Echinacea* extracts standardized with only one marker compound, particularly with only chicoric acid, will not exhibit any significant immunostimulatory activity. Applicants have herein clarified that the claimed method consists essentially of the recited steps and thus do not encompass a method that involves using more than either a chlorogenic or chicoric marker compound for standardizing an extract. Thus, one of ordinary skill in the art would not find the present invention, which teaches a method for selecting the maturation stage with the highest level of immune-stimulatory product and a standardized concentration of a marker compound, wherein the marker compound is either chlorogenic acid or chicoric acid, obvious in view of Gahler.

Additionally, when Gahler is viewed in connection with Rininger, as it must be, it is clear that one of ordinary skill in the art would have no reasonable expectation of success in achieving a method of obtaining an *Echinacea* extract having the highest level of immune-stimulatory compounds and a standardized concentration of chlorogenic or chicoric acid. Specifically, Rininger clearly teaches that the analyzed ***standardized*** extracts were "***inactive***" for immunostimulatory activity. *See* Rininger at pp. 505, 507, and 508. Furthermore, Rininger specifically analyzed chlorogenic acid and chicoric acid. Rininger teaches that *Echinacea* extracts that were ***standardized*** with either chlorogenic acid or chicoric acid as marker compounds were ***not*** found to possess any immunostimulatory activity. *Id.* Indeed, Rininger teaches, "standardized *Echinacea* extracts as well as purified chemical standards for the

production of *Echinacea* extracts were found to be inactive for these immunomodulatory functions." *Id.* at 508. This teaching is consistent with Rininger's analysis of ***non-standardized*** extracts. Rininger analyzed ***non-standardized*** *Echinacea* extracts and found that the ***non-standardized*** extracts possessed immunostimulatory activity. *Id.* at 507-8. Thus, one of ordinary skill in the art may fairly conclude from these teachings of Rininger that non-standardized extracts have immunostimulatory activity, but standardized *Echinacea* extracts do not possess immunostimulatory activity, particularly *Echinacea* extracts standardized with chlorogenic acid or chicoric acid as the marker compound.

The Office action argues against Applicants' reliance on Rininger to support its nonobviousness argument by arguing that Rininger does not teach that "all extracts" of *Echinacea* standardized for chicoric acid will be inactive for immunopotentiating activity. (Office action mailed 2/2/09, p. 13). Applicants respectfully maintain that Rininger provides a general teaching that non-standardized *Echinacea* extracts exhibit immunostimulatory activity while standardized extracts do not. Indeed, even Rininger's abstract teaches: "*Echinacea* extracts chemically standardized to phenolic acid or echinocaside content . . . were found to be inactive as immunostimulatory agents." Gahler does not change this teaching because Gahler itself teaches that *Echinacea* extracts standardized with only one marker compound, particularly with only chicoric acid, will not exhibit any significant immunostimulatory activity.

No Reasonable Expectation of Success Indicates the Nonobviousness of the Claimed Methods

Thus, Applicants respectfully submit that when the claims are considered in their entirety and when the references also are considered as a whole, without relying on impermissible hindsight, it is clear that the cited references do not provide any reasonable expectation of success in formulating a method for determining optimal harvest window of *Echinacea*, based on selecting a plant maturation

stage that has both a standardized concentration of either chicoric acid or chlorogenic acid as a marker compound that is obtained from the preparation of *Echinacea* plant for preparing a standardized extract, and that has immunostimulatory activity. Specifically, Seidler-Lozykowska and Dou both teach means for producing *Echinacea* extracts with the highest concentration of compounds used to standardize *Echinacea* extracts. Rininger teaches that neither standardized *Echinacea* extracts nor the common marker compounds used for standardization—particularly chlorogenic acid and chicoric acid—exhibit immunostimulatory activity. Gahler teaches that standardized extracts using multiple marker compounds in combination can produce immunostimulatory activity, but Gahler specifically teaches that *Echinacea* extracts standardized using chicoric acid do not have any significant immunostimulatory activity. Thus, one of skill in the art would not, based on the teaches of the cited references, expect the claimed method of optimizing harvest window of the *Echinacea* plant by selecting a plant maturation stage that has a standardized concentration of either chicoric acid or chlorogenic acid, yet also maintains immunostimulatory activity, to be successful.

Applicants also respectfully note that claims 3, 6-7, and 23-25 recite a specific standardization concentration of chicoric acid and are also nonobvious in view of this claimed concentration.

Claims 3, 6-7, and 23-25 are not obviousness in view of the cited references. Applicants have overcome these grounds of rejection and respectfully request that they be withdrawn.

CONCLUSION

Applicant believes that currently pending claims 3, 6-7, and 23-26 are patentable. The Examiner is invited to contact the undersigned attorney for Applicant via telephone if such communication would expedite allowance of this application.

Respectfully submitted,

/C. Noel Kaman/

C. Noel Kaman
Registration No. 51,857
Attorney for Applicant

BRINKS HOFER GILSON & LIONE
P.O. BOX 10395
CHICAGO, ILLINOIS 60610
(312) 321-4200